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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,793	PARANHOS-BACCALA ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *8-15,17-20,22-36 and 41-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,16,21,37-40 and 44-48* is/are rejected.

7)☒ Claim(s) *21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9-4-03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner handling this application has changed and is now Stephen Kapushoc in Art Unit 1634. Future correspondence regarding this application should be addressed to the above-mentioned Examiner.

Claims 1-48 are pending.

Claims 8-15, 17-20, 22-36, and 41-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-7, 16, 21, 37-40, 44-48 are examined on the merits.

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-7, 16, 21, 37-40, and 44-48) drawn to nucleic acid molecules in the reply filed on 02/02/2006 is acknowledged. The traversal is on the ground(s) that claims 1-48 are sufficiently related that a search and examination of the entire application cold be made without serious burden. This is not found persuasive because the separate classification of Groups I - VIII (as set forth in the restriction of 2/2/2005) is prima facie evidence that the examination of these inventions would place an undue burden on the examiner. Furthermore, the searches required to examine the different methods and the different products would be different (requiring a search of different classes, different electronic databases and the use of different key words in such a search). The search needed for the examination of the products is not coextensive with a search required for the methods; for example, a reference against a claimed nucleic acid or protein would not necessarily be a reference against a claimed method.

The requirement is still deemed proper and is therefore made FINAL.

Sequence Compliance

2. This application, 10/632,793, contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below:

The application contains sequences that are not identified by SEQ ID NOs and are not contained in the sequence listing of the application. For example, Figure 2 (pages 2/5 – 5/5 of the Drawings) contains a nucleic acid sequence and three translated reading frames that are not identified by SEQ ID NOs in either the Figure or a Brief Description of the Figures, and are not part of the sequence listing of the application.

In order to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), Applicant must submit, as appropriate, a new CRF and paper copy of the Sequence Listing containing the sequence, in addition to the previously listed sequences, an amendment directing the entry of the Sequence Listing into the specification, and a letter stating that the content of the paper and computer readable copies are the same. The specification should also be amended to include the appropriate SEQ ID NOs in the description of Fig. 2.

Claim note

2. Claim 21 is drawn to a product, but is dependent upon claims 10 and 19 which are drawn to methods. Prior to allowance of claim 21 it will be required to be amended so that it does not depend from non-elected claims.

Claim Objections

3. Claim 21 is objected to as specifically reciting non-elected subject matter. The Requirement for Restriction set forth on 02/02/2006 resulted in the election of a group including claim 21 as it pertains to a transcription product. The claim contains the phrase 'transcription/translation product'. Prior to allowance, non-elected subject matter will be required to be deleted from the claim.

Specification

4. The disclosure is objected to because of the following informalities:

The specification contains no section entitled Brief Description of the Drawings. Such a section should be included which contains a description of the provided figures, with reference to the appropriate SEQ ID NOs of any included sequence information.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7, 16, 21, 37-40, 44-48 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Because the claims read on polynucleotides that would occur in nature, untouched by the hand of man, these claims, as broadly drawn, encompass non-statutory subject matter. This rejection

may be overcome by amendment of the claims to include, for example, language clarifying that the claimed nucleic acids are intended to be isolated and/or purified nucleic acids.

Claim Rejections - 35 USC § 112 2nd Indefiniteness

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7, 16, and 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejected claims are unclear over the phrase 'not belonging to SEQ ID NO: 1 and encoding an expression product'. It is unclear if applicant intends that the claimed nucleic acid fragment specifically does not encode a transcription product. The claims may be made more clear by replacing the unclear phrase with 'not belonging to SEQ ID NO: 1, wherein said nucleic acid fragment encodes an expression product'.

Claim Rejections - 35 USC § 112 1st Enablement

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-7, 16, 21, 37-40, 44-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Although the rejected claims are drawn to products, this rejection is written to address the functional limitations that are recited in the claims and asserted in the specification (i.e. an association with disease). The specification does not provide nucleic acids associated with an autoimmune disease or with an unsuccessful pregnancy or pathological conditions of pregnancy.

Nature of the invention and breadth of the claims

The rejected claims are drawn to nucleic acids associated with an autoimmune disease, or with unsuccessful pregnancy or pathological conditions of pregnancy.

The claims encompass disease or pathological conditions in any organism.

Claims 1-7, 16, and 37-40 encompass nucleic acid fragments that are any portion of SEQ ID NO: 2 that does not belong to SEQ ID NO: 1 and encodes any expression product.

Claim 21 encompasses a transcription product that is any portion of any gag gene that encodes any expression product.

Claims 44, 47 and 48 encompass nucleic acid fragments that are any part of any gag gene that encodes any gag protein.

Claims 5, 37, 39 and 47 require that the nucleic acid is associated with an autoimmune disease.

Claims 6, 38, 40 and 48 require that the nucleic acid encode an expression product that is recognized by antibodies present in a biological sample from a patient suffering from multiple sclerosis.

The nature of the invention requires knowledge of an association between a nucleic acid fragment and a disease or pathological condition.

Direction provided by the specification and working example

The specification of the instant application describes the identification of a retroviral-like gene structure, named 'HERV-W' by the applicant, in a placental cDNA library by testing with Ppol-MSRV (SEQ ID NO: 18) and Penv-C15 (SEQ ID NO: 19) probes and then carrying out gene walking (p.3 lns. 1-10).

The specification of the instant application teaches that applicant envisages the potential role of retroviral type structures in the development of autoimmune disease, in unsuccessful pregnancy or pathological conditions of pregnancy (p.2 lns.18-24).

The specification teaches the sequences of several clones that contain various retroviral-like elements (p.3 lns. 15-35); the specification further teaches that the different clones were subject to sequence alignment to create a putative genetic organization of HERV-W in the RNA form (SEQ ID NO: 30) (pp.4-5).

The specification teaches that homology searching over several databases using 'the reconstructed genome' (presumably SEQ ID NO: 30) identified several related sequences in the human genome. The specification provides a diagrammatic view of the alignment of four clones with the 'reconstructed genome' (Fig 1), and indicates that the reconstructed genome is contained entirely within clone RG083M05 (p.6 ln.13). The

specification further teaches that RG083M05 is 96% similar to the reconstructed genome, but indicates that no genomic fragments identified by database searching contained a 'functional gag gene' (p.6 lns.19-20).

The specification further teaches the production of the 'Pgag-C12' probe (SEQ ID NO: 3), which corresponds to the coding region of the clone MSRV gag c12 (Example 1, pp. 10-14). The specification teaches amplification of the MSRV gag gene by RT-PCR from total RNA extracted from plasma from a patient suffering from MS. The specification teaches using the MSRV gag gene probe in a Southern blot analysis (Monochromosomal Somatic Cell Hybrid blot) to identify gene location and copy number.

In is not clear if applicant intends that amplification of the 'MSRV gag c12' probe creates a nucleic acid sequence equivalent to the 'HERV-W gag gene' of the instant application. In fact, an alignment of the former (SEQ ID NO: 3; p.13 ln.9) with the latter (SEQ ID NO: 2; p. 18 ln 35; the claims are specifically drawn to SEQ ID NO: 2) indicates that the two sequences are not identical.

The specification does not teach the amplification any gag gene by RT-PCR other than the single example of amplification of the MSRV gag gene from the plasma of an MS patient (example 1). The specification does not teach any amplification from any non-MS patient.

The specification describes the amplification of the HERV-W gag gene from isolated human chromosomes (example 2.1), and subsequent analysis of the

amplification product by agarose gel and hybridization of the amplification product with the gag c12 probe. The specification does not provide the results of this analysis.

The specification teaches that the PCR products created from the amplification of HERV-W gag genes from individual chromosomes were subjected to in vitro transcription/translation, and the protein products were analyzed by gel electrophoresis. The results indicate that the PCR products of the amplified HERV-W gag gene from chromosomes 1, 3, 6, 7, and 16, upon in vitro transcription/translation, produced proteins of molecular masses ranging from 17-45 kDa (Example 2.2; Table 2).

The specification provides no analysis of the transcription/translation beyond the molecular masses (Table 2) of the protein products. The specification teaches that SEQ ID NO: 2 encodes a protein of approximately 45 kDa (p.22 ln.15); there is no indication as to the source of the mass heterogeneity in the transcription/translation products using the PCR templates. Given the heterogeneity of the products resulting from in vitro transcription/translation, it is notable that there is no analysis of the actual amino acid sequences of any of the protein products; though the specification teaches that the PCR products used as templates for in vitro transcription/translation were sequenced (p.18 lns.21-32) the specification does not provide the results of the nucleic acid sequence analysis.

The specification further teaches the production of a recombinant protein from an expression vector containing the coding region of SEQ ID NO: 2, and reaction of sera with the recombinant protein (Example 3). The results (Table 3) indicate that 6 of 15 'MS', 1 of 2 'Neurological Controls', and 1 of 22 'Healthy Controls' samples showed

reactivity to the recombinant protein. The results provide only a qualitative measure of reactivity (i.e.: +++, ++, +, +/-). There is no definition of what is the source of a sample that is a 'Neurological control'. There is no statistical interpretation of the data to examine the significance of the results.

The specification does not provide any analyses related to any diseases other than multiple sclerosis. There is no analysis of biological samples from patients suffering from any other autoimmune disease. There are no analyses pertaining to biological samples related to unsuccessful pregnancy or any pathological conditions of pregnancy.

There is no analysis of any fragments of SEQ ID NO: 2. Notably, there is no indication of the different expression of any transcription or translation product belonging to SEQ ID NO: 2 but not SEQ ID NO: 1.

The specification provides no analysis of any nucleic acids or transcripts in a disease sample (e.g. autoimmune disease or pathological condition of pregnancy) as compared to any non-disease control sample.

State of the art, level of skill in the art, and level of unpredictability

While the state of the art with regard to identification or production of any nucleic acid of a particular sequence is high, the unpredictability of associating any specific nucleic acid or nucleic acid fragment with a particular pathological condition is even higher.

The prior art does not teach the association of nucleic acid fragments of SEQ ID NO: 2 encoding a portion of a gag gene but not belonging to SEQ ID NO: 1 as being

associated with any disease in a statistically significant manner. Given the requirements of claim 1 (and thus the dependent claims 2-7, 16, 37-40), that the nucleic acid fragment encode a portion of the gag gene, and is a fragment of SEQ ID NO: 2 but not SEQ ID NO: 1, and the extremely high degree of identity between SEQ ID NO: 2 and SEQ ID NO: 1 (Blast 2 sequences results: Align Seq ID 1:2), the claims appear to be drawn to a sequence related to positions 374-473 of SEQ ID NO: 2. There is no indication in either the specification or the prior art that this sequence is associated with any disease or any pathological condition.

While the claims encompass nucleic acid fragments associated with disease and pathologies in any organism, the specification teaches the analysis of nucleic samples only from humans. The prior art of Mayer et al (1998) teaches that related sequences (e.g. the sequence of a gag gene from an endogenous retrovirus) are different among several closely related species, including Humans, green monkeys, and macaque (p.1872 – Sequencing of HERV-K gag genes from lower Old World primates; Fig 6). Thus it is unpredictable as to whether or not the claimed nucleic acid fragments would be applicable to any species other that humans.

The specification teaches the amplification of RNA sequences from samples via RT-PCR. It is, however, not taught that the presence of a nucleic acid in the genome (DNA gene) or expression of the nucleic acid (RNA transcript) is associated with a disease. The post-filing art of Newton et al (2001) teaches the difficulty in applying gene expression results to the association of gene expression with a phenotype. Newton et al teaches that a basic statistical problem is determining when the measured

differential expression is likely to reflect a real biological shift in gene expression, and replication of data is critical to validation (p.38, third full paragraph). The specification teaches only the analysis of sera reactivity to recombinant protein. However it is unpredictable as to whether or not such a measure of protein levels is indicative of any nucleic acid expression. The post-filing art of Chan teaches that cells have elaborate regulatory mechanisms at the level of transcription, post-transcription, and post-translation (p1, last paragraph), and that transcript and protein abundance measurements may not be concordant (p.3, sixth full paragraph). Thus it is unpredictable as to whether or not the claimed nucleic acid fragment or transcription product is associated with any disease or pathological condition.

While the specification asserts that the claimed sequence has potential role in the development of autoimmune disease, in unsuccessful pregnancy or pathological conditions of pregnancy (p.2 lns.18-24), there is a lack of evidence presented to indicate any association of the sequence to such pathologies. The post-filing art reveals that most gene association studies are typically wrong. Lucentini (2004) teaches that it is strikingly common for follow-up studies to find gene:disease associations wrong (left column, 3rd paragraph). Lucentini teaches that two recent studies found that typically when a finding is first published linking a given gene to a disease there is only roughly a one-third chance that the study will reliably confirm the finding (left column, 3rd paragraph). Lucentini teaches that bigger sample sizes and more family-based studies, along with revising statistical methods, should be included in gene association studies (middle column, 1st complete paragraph). And while the instant specification provides

no statistical analysis regarding the sera reactivity of different samples to a recombinant protein encoded by SEQ ID NO: 2, the prior art of Thisted (1998) provides guidance as to what is required to indicate that an association is statistically significant. Thisted teaches that it has become scientific convention to say that a p-value of 0.05 is considered significant (p.5 - What does it mean to be 'statistically significant'), and that values above the conventional reference point of 0.05 would not be considered strong enough for the basis of a conclusion.

Quantity of experimentation required

A large and prohibitive amount of experimentation would have to be performed in order to make and use the claimed invention. One would have to perform a large case:control study to examine the large genus of claimed nucleic acid sequences to determine whether or not any claimed sequence is in fact a gag gene of an endogenous retrovirus associated with a disease. This would involve the analysis of many possible different organisms, and also the examination of a large number of diseases. Because of the breadth of the claims as written, one would have to investigate an enormous number of nucleic acid fragments, which minimally need only contain any protein encoding portion of SEQ ID NO: 2, which could be a nucleic acid fragment as few as three nucleotides.

Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the lack of guidance by the applicant and the paucity of

working examples, it is the conclusion that an undue amount of experimentation would be required to make and use the invention as intended.

Claim Rejections - 35 USC § 102

The claims of the instant application are broadly drawn to nucleic acid fragments. In examination of the claims, the recitation of an intended use is not considered a significant limitation of the claim. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim (see MPEP 2112).

Additionally, it is noted that the claim limitations that characterize a nucleic acid fragment as 'encoding an expression product' are interpreted as broadly as they are written. All polynucleotides encode expression products in so far as all polynucleotides may be transcribed e.g. to create an RNA expression product), and all RNA expression products that comprise an amino acid encoding triplet codon may be translated (to create a polypeptide expression product).

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6, 16, 37, 38, and 44-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796) (1995).

Brennan teaches a microarray that contains 10-mer polynucleotides spotted at a discrete locations such that the total array represents every possible permutation of 10-

mer oligonucleotide (col. 9, lns. 48-55). Such an array would inherently comprise any 10-mer nucleic acid, including nucleic acids claimed in the instant application.

Regarding claim 1, the array of Brennan, due to its comprehensive nature, includes a 10-mer of the sequence GGAAACATTC. Such a sequence is identical to nucleotides 377-386 of SEQ ID NO: 2, which are not contained in SEQ ID NO: 1, and encode the amino acids Gly Asn Ile.

Regarding claims 2-3, the array of Brennan contains the nucleic acids of claim 1 which are inherently present in chromosome 3.

Regarding claim 4, the probe array of Brennan contains DNA probes, which encode messenger RNA sequences.

Regarding claims 5 and 6, the array of Brennan, due to its comprehensive nature, contains nucleic acids that encode a portion of the gag gene recognized by antibodies present in a biological sample from a patient suffering from multiple sclerosis.

Regarding claim 16 the nucleic acid array of Brennan comprises the fragment of claim 1, and due to it comprehensive nature would be suitable for the detection of a nucleic acid in a biological sample.

Regarding claims 37 and 38, the array of Brennan includes nucleic acids that meet the limitations of claim 1, thus if the retroviral elements of the instant application are associated with multiple sclerosis, then the nucleic acid fragments of Brennan are also associated with multiple sclerosis.

Regarding claims 44-48, the claims encompass nucleic acid fragments that encode 'a gag protein'. Neither the claims nor the specification define the requirements

of 'a gag protein', which in the examination of the claims is interpreted to mean any portion of the amino acid sequence of SEQ ID NO: 31. Due to its comprehensive nature the array of Brennan includes nucleic acid fragments that encode part of the gag gene of an endogenous retrovirus associated with an autoimmune disease, and the part of the gene includes the portion of the gag gene that encodes a gag protein, relevant to claim 44. Relevant to claims 45 and 46, the array of Brennan includes all possible 10-mers, thus teaches fragments including series of contiguous nucleotides of SEQ ID NO: 2 including portions that encoded a gag protein. Relevant to claims 47 and 48, the array of Brennan includes every 10-mer oligonucleotide, thus teaching nucleic acid fragments that encode part of the gag gene of an endogenous retrovirus associated with a multiple sclerosis, which is an autoimmune disease.

12. Claims 7, 16, 21, 39, 40, and 44-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Mayer et al (1998).

Mayer et al teaches a nucleic acid fragment consisting of part of the gag gene of an endogenous retrovirus. The nucleic acid of Mayer et al satisfies all of the structural limitations of the claims. Given the lack of a definition of the phrase 'associated with an autoimmune disease, or with unsuccessful pregnancy of pathological conditions of pregnancy' in either the claims or the specification, the nucleic acid taught by Mayer et is considered to meet this claim limitation. The MPEP in chapter 2100 states:

> Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best,

562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Regarding claim 7, Mayer et al teaches amplification of a gag gene (p.1871 - PCR primers and conditions), and subjecting the resulting PCR product to in vitro transcription/translation (p.1871 – PTT) which creates a transcription product. The claim requires that the transcript be at least a portion of the gag gene of a fragment according to claim 1. In the Mayer reference the transcription product includes transcription of the nucleotides ATGGG (as described in the T7gagFOR primer (p.1871 - PCR primers and conditions)). These nucleotides satisfy the limitations of a fragment according to claim 1 in that they are one portion of the gag gene, and are a series of contiguous nucleotides belonging to SEQ ID NO: 2 but not SEQ ID NO: 1, and encode and expression product.

Regarding claim 16, the full length HERV-Kgag PCR product taught by Mayer et al is a detection reagent comprising at least one fragment that satisfies the limitation of claim 1. The PCR product comprises the nucleotides ATGGG (as described in the T7gagFOR primer (p.1871 - PCR primers and conditions)). These nucleotides satisfy the limitations of 'a fragment according to claim 1' in that they are one portion of the gag gene, and are a series of contiguous nucleotides belonging to SEQ ID NO: 2 but not SEQ ID NO: 1, and encode and expression product.

Regarding claim 21, Mayer et al teaches the amplification of a full length gag gene (p.1871 - PCR primers and conditions), and subjecting the resulting PCR product to in vitro transcription/translation (p.1871 – PTT) which creates a transcription product.

Thus the reference teaches a detection reagent comprising at least one transcription product.

Regarding claims 39 and 40, Mayer et al teaches a transcription product that satisfies all of the structural limitations of the claims, as described in the rejection of claim 7. As explained earlier in this rejection given the lack of a definition of the phrase 'associated with an autoimmune disease, or with unsuccessful pregnancy of pathological conditions of pregnancy' in either the claims or the specification, the nucleic acid taught by Mayer et is considered to meet this claim limitation as set forth in the base claim (claim 1).

Regarding claim 44, Mayer et al teaches a nucleic acid fragment (Fig 6) that consists of part of the gag gene of an endogenous retrovirus. Mayer et al teaches that the fragment of Fig. 6 is the central portion of the gag gene that map to nucleotides 1626 to 2261 of the HERV-k10 sequence, which is a part of the gag gene that includes at least the portion of the gag gene that encodes a gag protein. The lack of a definition of the phrase 'associated with an autoimmune disease, or with unsuccessful pregnancy of pathological conditions of pregnancy' in either the claims or the specification, the nucleic acid taught by Mayer et is considered to meet this claim limitation.

Regarding claims 45 and 46, reading the claims as broadly as they are written, the sequence of Mayer et al includes a series of contiguous nucleotides from SEQ ID NO: 2 (relevant to claim 45) that encodes a gag protein (relevant to claim 46). For example, SEQ ID NO: 2 contains the nucleotides CCC (positions 446-448 of SEQ ID NO: 2) which encode a proline amino acid, and the sequence of Fig. 6 includes the

serioes of nucleotides CCC (for example at postions 97-99 of the K10gag sequence in Fig 6).

Regarding claims 47 and 48, as explained earlier in this rejection given the lack of a definition of the phrase 'associated with an autoimmune disease, or with unsuccessful pregnancy of pathological conditions of pregnancy' in either the claims or the specification, the nucleic acid taught by Mayer et is considered to be a nucleic acid from an endogenous retrovirus associated with multiple sclerosis, which is an autoimmune disease.

13. Claims 1-7, 16, 21, 37-40, and 44-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Perron et al WO 98/23755 (1998).

Perron et al teaches viral material and nucleotide fragments associated with multiple sclerosis (p.8 lns.13-15). The reference includes nucleic acid fragments that satisfy the limitations of the rejected claims.

Regarding claim 1, Perron et al teaches an oligonucleotide with the sequence 5'-TGT CCG CTG TGC TCC TGA TC-3' (SEQ ID NO: 139, p.198, lns.10-18). This sequence is identical to positions 87-106 of SEQ ID NO: 2, which are not in SEQ ID NO: 1. The sequence is a nucleic acid which encodes an expression product; the nucleotides encode an RNA transcript (which is an expression product) of the sequence 5'-UGU CCG CUG UGC UCC UGA UC-3', and a polypeptide (which is an expression product) of the sequence VRCAPD (in reading frame 2).

Regarding claims 2 and 3, the nucleic acid fragment of SEQ ID NO: 139 from Perron et al is inherently associated with chromosome 3.

Regarding claim 4, the RNA sequence encoded by SEQ ID NO: 139 of Perron et al is structurally identical to a messenger RNA of the same sequence.

Regarding claims 5 and 6, the polypeptides encoded by SEQ ID NO: 139 of Perron et al are of a sufficient size to be recognized by antibodies. Given the lack of an defining parameters for the claim limitation 'immunologically recognized', the encoded polypeptides are expression products that can be immunologically recognized by antibodies in a sample from a patient suffering from multiple sclerosis, which is autoimmune disease.

Regarding claim 7, Perron et al teaches that SEQ ID NO: 139 is a cDNA molecule (p.198 ln.16). Because cDNA are reverse transcribed from RNA, the reference teaches a transcript that comprises the nucleic acid sequence of SEQ ID NO: 139, which is a fragment according to claim 1.

Regarding claim 16, SEQ ID NO: 139 of Perron is a detection reagent comprising a fragment according to claim 1.

Regarding claim 21, Perron et al teaches that SEQ ID NO: 139 is a cDNA molecule (p.198 ln.16). Because cDNA is reverse transcribed from RNA, the reference teaches a transcript that comprises the nucleic acid sequence of SEQ ID NO: 139. Such a transcript is structurally identical to the claimed transcription product.

Regarding claims 37 and 38, the nucleic acid fragment SEQ ID NO: 139 of Perron et al satisfies the limitations of claim 1. Thus if the retroviral elements of the

instant application are associated with multiple sclerosis, then the nucleic acid fragments the reference are associated with multiple sclerosis.

Regarding claims 39 and 40, as indicated in the rejection of claim 7, Perron et al teaches a transcription product of the sequence corresponding to SEQ ID NO: 139. The nucleic acid fragment of Perron et al satisfies the limitations of claim 1. Thus if the retroviral elements of the instant application are associated with multiple sclerosis, then the nucleic acid fragments the reference are associated with multiple sclerosis.

Regarding claim 44, Perron et al teaches SEQ ID NO: 88 (p.177) that consists of part of a gag gene of MSRV-1 (Example 12, pp.75-77), and encodes a gag protein (Fig 36). The reference teaches that the gene is from the MSRV-1 virus, which is associated with an autoimmune disease (Example 17, pp.87-97).

Regarding claims 45 and 46, the nucleic acid fragment taught by SEQ ID NO: 88 of Perron et al includes a series of contiguous nucleotides from SEQ ID NO: 2 of the instant application that encode a gag protein. For example, nucleotides 64-96 of SEQ ID NO: 88 are identical to nucleotides 851-883 of SEQ ID NO: 2. This is a portion of the gene that encodes a protein.

Regarding claim 47 and 48, the reference teaches the association of the virus with multiple sclerosis, which is an autoimmune disease (Example 17, pp.87-97).

Conclusion

14. No claim is allowable. No claim is free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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